44. (Twice Amended) The method of claim 25, wherein said particulate carriers comprise:

(a) liposomes comprising a pharmaceutically acceptable liposome membrane forming substance; and

b) a 0.1 to 2% PVP iodine solution, wherein the liposomes are in a size range between about 50 nm and about 4,000 nm.

45. (Twice Amended) The method of claim 44, wherein the liposomes are in a gel.

51. (Amended) The method of claim 25, wherein the particulate carriers have a size in the range between about 50nm and about 4,000nm diameter.

52. (Amended) The method of claim 25, wherein the particulate carriers have a size in the range between about 500 nm and 2,500 nm diameter.

53. (Amended) The method of claim 25, wherein the particulate carriers have a size of about 1,000nm diameter.

REMARKS

Claims 25-26, 29-47 and 51-53 are pending. Claims 1-24, 27-28 and 48-50 have been canceled without prejudice. It is respectfully submit that no new matter has been added by virtue of this amendment.

I. RENUMBERING OF CLAIMS

In the Office Action, the Examiner indicated that claims were renumbered according to rule 126 since claims 26, 31, 33, 38 and 45 missing. In response, the Examiner is directed to pages 31-33 and 35 of the specification as filed which recites claims 26, 31, 33, 38 and 45. Accordingly, the Examiner is requested to further examine the claims in view of the original

numbering.

II. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

In the Office Action, the Examiner rejected claims 1-48 under 35 U.S.C. § 112, first paragraph for lack of enablement. The Examiner stated that the "instant specification does not provide adequate support for the broadly claimed 'antiseptic', anti-inflammatory agents and wound healing promoting agents and 'particulate carrier'' for example claim 27 defines an anti-inflammatory agent as antiseptic, antibiotic, corticosteroid and wound healing promoting agent; the specification also does not adequately describe what 'functional and cosmetic tissue remodeling' is and how the method is practiced as claimed in the method claims. Instant specification also does not teach how one can apply topically to the respiratory tract and treat or prevent diseases such as HIV and opportunistic diseases."

In response, the claims have been amended as not to recite a "generic agent". The claims as amended, are now directed to antiseptic or wound healing agents. It is respectfully submitted that the pending claims do provide adequate support for these claim terms.

With respect to antiseptic agents, the Examiner is directed to page 5, lines 13-16, which states that "antiseptic agents are understood to include those disinfecting agents which are pharmaceutically acceptable and suitable for the upper respiratory tract..." Further, page 5, lines 18-23 provides specific examples of antiseptic agents which are known to one skilled in the art.

With respect to wound healing agents, the Examiner is directed to page 5, lines 25-27 which defines such agents as agents which promote granulation and epithelization. This is followed by specific examples of wound healing agents which are known to one skilled in the art.

With respect to "functional and cosmetic tissue remodeling" the Examiner is directed to page 6, line 11 to page 7, line 4 which states the following:

> *...it is known that body tissue repair may be accompanied by the formation of scar tissue, which can be functionally and/or cosmetically harmful, or at least undesirable. Hyperkeratosis and the uncontrolled proliferation of tissue may cause serious harm, leading to dysfunctions, and may of course also be cosmetically undesirable. After infections and inflammations, re-growing or healing tissue may cause neoplasms and intergrowth...*

In view of this teaching in the specification, it is submitted that one skilled in the art would understand the meaning of the term "functional remodeling" as tissue repair and tissue growth produced in the location of a previous infection, lesion or open wound which results in, e.g., restored blood flow to an injured area; and the term "cosmetic remodeling" results when previously damaged tissue is repaired so that scarring, e.g., hyperkeratosis, is reduced or prevented, therefore, leaving little or no visible signs of previous damage. However, to advance the prosecution of the application, the term "cosmetic" has been removed from the pending claims.

With respect to the Examiner's statement that the "specification also does not teach how one can apply topically to the respiratory tract and treat or prevent diseases such as HIV and opportunistic diseases", the Examiner is directed to page 7, line 6-29, page 11, lines 8-27 and page 12, lines 4-12 and page 20, lines 15-22, wherein specific administration routes and dosage forms are described. These include respiratory tract administration via nebulization or dry powder inhalation via pneumatic pump applicators, two-chamber gas pressure packs, aerosol spray dispensers. Further, it is pointed out to the Examiner that the presently claimed invention and methods cannot be used to prevent diseases such as HIV, but rather to treat and alleviate such diseases, e.g., by treating opportunistic infections which are known to one skilled in the art

to be associated with such diseases as set forth on page 11, lines 22-27 of the specification.

In view of the arguments presented, it is respectfully submitted that the present application enables one skilled in the art to practice the present invention as recited in the claims and the Examiner is requested to remove the § 112, first paragraph rejections.

III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH:

In the Office Action, the Examiner rejected claims 1-48 under 35 U.S.C. § 112, second paragraph, as being indefinite on several grounds:

With respect to the rejection on the grounds that "it is unclear what applicant intends to convey by healing wounds to the upper respiratory tract," the Examiner is directed to page 6, lines 11-20, which describes problems associated with tissue repair and the need for proper wound healing in order to prevent or reduce scarring and hyperkeratosis associated with wounds which can be present in the upper respiratory tract due to, e.g. upper respiratory infections.

With respect to the rejection on the grounds that "the distinction between the anti-inflammatory agent, antiseptic and wound healing promoting agent in claim 1 is unclear" the Examiner is directed to page 5, lines 13-27 which describes that "antiseptic agents" are agents which are disinfecting agents and "wound-healing agents" are agents which promote granulation and epithelization. The term "anti-inflammatory" has been deleted from the claims.

With respect to the rejection on the grounds that "the distinction between liposomes and microspheres and nanoparticles in claim 2 is unclear" it is respectfully submitted that these terms are known to one skilled in the art as separate and distinct carrier particles. Microspheres are known in the art from, e.g., WO 95/15118, as set forth in the specification on page 9, lines 9-12 and nanoparticles are known in the art as described by Heyder, as set forth on page 9, lines 14-18 of the specification.

With respect to the terms "greatest", "such as", "including", and "in case", the claims have been amended to delete these terms.

With respect to the rejection of claims 4-6, 7-8 and 29 (rejected in the Office Action as claim 28) based on improper Markush format, the claims have been amended to proper Markush format.

With respect to the rejection of the terms "conserving agents" and "consistency forming agents", it is respectfully submitted that one skilled in the art would understand these terms as encompassing pharmaceutically acceptable excipients which provide the designated function.

With respect to the rejection of claim 15, this claim has been canceled.

With respect to the rejection of claims 1 and 20, these claims have been deleted. In response to the Examiner's inquiry "how can a particulate carrier be in solution" with respect to claim 44, which is similar to claim 20, it is submitted that it is known to one skilled in the art that a particulate carrier, e.g., a liposome, can be contained in a liquid or semi-solid medium, e.g., a gel or cream.

With respect to the rejection of claims 5, 16, 22, 23 and 28 (rejected in the Office Action as claim 27) claims 5, 16, 22, 23 and 28 have been canceled.

With respect to the rejection of claim 23 and 47 (rejected in the Office Action as claim 42), the term "angina" has been deleted.

With respect to the rejection of claims 24 and 25, claims 24 and 25 have been canceled. However, new claim 54 has been added to recite, in pertinent part, "functional tissue remodeling." "Functional tissue remodeling" is described in the specification from page 6, lines

11-20 as tissue repair and tissue growth produced in the location of a previous infection, lesion or open wound which results in, e.g., restored blood flow to an injured area. "Cosmetic remodeling" has been deleted from the present claims.

With respect to the rejection of claim 40, one skilled in the art would recognize that the terms O/W or W/O refer to oil-in-water and water-in-oil emulsions, respectively. Oil-in-water emulsions are have an oleaginous internal phase and an aqueous external phase. Conversely, water-in-oil emulsions have an aqueous internal phase and an oleaginous external phase.

In view of the arguments presented, it is respectfully submitted that the present application enables one skilled in the art to practice the present invention as recited in the claims and the Examiner is requested to remove the § 112, second paragraph rejections.

IV. DOUBLE PATENTING REJECTION:

In the Office Action, claims 1-48 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-57 of copending Application No. 09/701,450 and claims 1-24 and 43-45 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 5,863,556.

In response, Applicants submit that upon indication that the claims are otherwise allowable, the filing of terminal disclaimers will be considered.

V. REJECTION UNDER 35 U.S.C. § 102(b):

In the Office Action, the Examiner rejected claims 1-4, 9-12, 14-16, 19-28, 31-33, 35-36, 39 and 41-48 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,049,388 ("the Knight patent"). The Examiner stated that "Knight discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include

antibiotics, antiviral agents and steroids...."

Claims 1-4, 9-12, 14-16, 19-28, 31-33, 35-36, 39 and 41-48 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,049,389 ("the Radhakrishnan patent). The Examiner stated that Radhakrishnan discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids...."

Claims 1-4, 9-12, 14-16, 19-28, 31-33, 35-36, 39 and 41-48 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,290,540 ("the Prince patent). The Examiner stated that Prince discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-10 microns. The drug combination include antibiotics, antiviral agents and steroids...."

In response, composition claims 1-4, 9-12, 14-16 and 19-24 have been canceled. With respect to the pending method claims, these claims are directed to methods of treatment comprising administering to the ears, nose or throat compositions comprising antiseptic agents or agents which promote the healing of wounds. It is respectfully submitted that neither the Knight patent, the Radhakrishnan patent nor the Prince patent teach or suggest antiseptic agents or agents which promote the healing of wounds in the methods described therein. Accordingly, the claims are not anticipated by these references and the Examiner is requested to withdraw these rejections.

In the Office Action, the Examiner rejected claims 1-24 and 43-48 under 35 U.S.C. § 102(b) as being anticipated by JP-7145081 or EP- 0939373. The Examiner stated "JP and EP both disclose the same composition...The intends [sic] use has no patentable significance in the composition claims."

This rejection is respectfully traversed. The JP and EP references disclose liposomal preparations useful in the treatment of external wounds. These references do not teach or suggest the compositions disclosed therein as useful for treatment of the ears, nose or throat as encompassed by the independent method claims of the present invention. Accordingly, the Examiner is requested to remove the anticipation rejections over these references.

V. REJECTION UNDER 35 U.S.C. § 103(a):

In the Office Action, the Examiner rejected claims 25-42 and 46-48 under 35 U.S.C. § 103(a) as being unpatentable over the Knight or the Radhakrishnan or the Prince patents. The Examiner stated that "Knight, Radhakrishnan and Prince do not teach the administration of the composition for the infections which occur during cosmetic surgery. However, it is deemed obvious to one of ordinary skill in the art that the wound healing compositions can be applied during any state wherein the wounds are susceptible to infectious agents, with the expectation of similar anti-septic effect."

This rejection is respectfully traversed, at the very least, as the claims are directed to methods of treatment comprising administering to the ears, nose or throat compositions comprising antiseptic agents or agents which promote the healing of wounds as disclosed in the specification. It is respectfully submitted that neither the Knight patent, the Radhakrishnan patent nor the Prince patent teach or suggest antiseptic agents or agents which promote the healing of wounds in the methods described therein. Accordingly it would not be obvious in view of these references to utilize such compositions in the presently claimed methods.

In the Office Action, the Examiner rejected claims 25-42 and 46-48 under 35 U.S.C. § 103(a) as being unpatentable over JP or EP in combination with Knight or Radhakrishnan or Prince.

These rejections are respectfully traversed, at the very least, as the JP and EP references are not properly combinable with either the Knight, Radhakrishnan and Prince references. The JP and EP references are directed to external treatments, while the secondary references are directed to pulmonary treatment. Accordingly, one skilled in the art would not be motivated to combine these references. Accordingly, the Examiner is requested to remove the rejection under 35 U.S.C. § 103(a).

CONCLUSION:

Applicants respectfully submit that in view of the amendments made and arguments presented, the present application is in condition for allowance.

A check in the amount of $1160.00 is enclosed, $980.00 of which is for the petition for three-month extension of time. If it is determined that additional fees are due or that any fee has been overpaid, the Commissioner for Patents is hereby authorized to charge said fee or credit any overpayment to Deposit Account No. 50-0552.

Respectfully submitted,

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MARKED-UP VERSION OF AMENDED SPECIFICATION

On page 4, please **replace** paragraph 4 (lines 13-16) with the following:

- - An object of the instant invention is to provide a well tolerated, easily applicable, anti-inflammatory, especially antiseptic and/or wound-healing promoting preparation, which provides protracted release and protracted topical effect of the active agent in the upper [lower] respiratory tract. - -

On page 9, please **replace** paragraph 3 (lines 14-18) with the following:

- - Nanoparticles may in some case be used, provided that they can be loaded with a sufficient amount of active agent and can be administered to the upper [lower] respiratory tract according to this invention. They can be prepared according to the methods known in the art, as e.g., described by Heyder (GSF München) in "Drugs delivered to the lung, Abstracts IV, Hilton Head Island Conference, May 1998.

MARKED-UP AMENDED CLAIM VERSION

25. (Twice Amended) A method of [preventing or] treating infections of [functional and cosmetic tissue remodeling and repair, of] the ears, nose or throat in a human or animal [upper respiratory tract or ear, by applying to said tract or ear, a pharmaceutical preparation] comprising administering to the ears, nose or throat, a pharmaceutical preparation comprising particulate carriers combined with an agent selected from the group consisting of [at least one anti-inflammatory,] an antiseptic agent, [or] a wound-healing promoting agent[, said at least one agent being combined with a particulate carrier in the preparation] or a combination thereof.

26. (Amended) The method of claim 25, wherein said particulate carriers [carrier] [comprises at least one] are selected from the group consisting of a liposome preparation, a microsphere preparation, a nanoparticle preparation, a Large Porous Particle preparation [or] , a laser-pulse polymer coated molecule preparation and a combination thereof.

29. (Twice Amended) The method of claim 25, wherein the antiseptic agent is selected from the group consisting of oxygen- releasing compounds, [and] halogen-releasing compounds[;] , metal compounds, [such as silver compounds, mercury compounds;] organic disinfectants [including formaldehyde-releasing compounds], alcohols, phenols [including alkylphenols arylphenols as well as halogenated phenols], quinolines, acridines, hexahydropyrimidines, quaternary ammonium compounds, iminium salts, [and] guanidines, and combinations thereof.

30. (Twice Amended) The method of claim 25, wherein the antiseptic agent is selected from the group consisting of [comprises] metal compounds [such as mercury compounds], phenols, phenol derivatives, [such as thymol, eugenol, hexachlorophene] iodine, [and] iodine complexes and combinations thereof.

32. (Twice Amended) The method of claim 25, wherein the wound-healing promoting agent is selected from the group consisting of [comprises agents promoting granulation and epithelization such as] dexpanthenol, allantoines, azulenes, tannines, [or compounds from the] vitamin B [series] compounds and combinations thereof.

34. (Twice Amended) The method of claim 25, wherein the particulate carriers have [carrier particles has] a [substantially uniform] size in the range between about 20nm and about 20,000 nm diameter.

36. (Twice Amended) The method of claim 25, wherein [that] the [carrier] preparation releases the agent at approximately the same release rate over the release time period.

39. (Twice Amended) The method of claim 25, wherein the preparation is in the form of a solution [or dispersion comprising the active-agent loaded carrier in the form of a liquid pharmaceutical preparation].

40. (Twice Amended) The method of claim 25, wherein the preparation is in the form of a hydrophilic or amphiphilic cream, [comprising the carrier and agent formulation in a hydrophilic or amphiphilic cream base, or in the form of a pharmaceutical O/W or W/O] an oil in water lotion or a water in oil lotion.

43. (Twice Amended) The method of claim 25, wherein the preparation is in the form of a [spray containing the carrier and agent in a pharmaceutically acceptable sprayable] solid or liquid [formulation] spray.

44. (Twice Amended) The method of claim 25, wherein the particulate carriers [preparation is in the form of a pharmaceutical solution or dispersion formulation, which comprises] comprise:

(a) liposomes comprising [compromising] a pharmaceutically acceptable liposome membrane forming substance; and

(b) a 0.1 to 2% PVP iodine solution [at approximately 10% available iodine in the PVP iodine complex at least most of which is encapsulated by said liposome membranes], wherein the liposomes are [of substantially uniform] in a size between about 50 nm and about 4,000 nm[, and, in case, the formulation additionally comprises customary additives, adjuvants and auxiliary substances of a pharmaceutical solution or dispersion formulation].

45. (Twice Amended) The method of claim [25] 44, wherein the liposomes are in [of substantially uniform size, with diameters at around 1,000 nm, and the preparation is] a gel.

47. (Twice Amended) The method of claim 25, wherein the preparation is suited for the treatment of acute laryngopharyngitis, chronic laryngopharyngitis, [angina] or rhinitis.

51. (Amended) The method of claim 25, wherein the particulate carriers [carrier particles comprise] have a [has a substantially uniform] size in the range between about 50 nm

and about 4,000 nm diameter.

52. (Amended) The method of claim 25, wherein the particulate carriers [carrier particles comprise] have a [substantially uniform] size in the range between about 500 nm and 2,500 nm in diameter.

53. (Amended) The method of claim 25, wherein particulate carriers [carrier particles comprise] have a [uniform] size of about 1,000 nm diameter.